reflects the increased efficiency of parenteral fluid administration in recent years.

Though the mortality in this series compares favourably with most of the published works, some of the deaths could have been prevented by more rigorous patient selection, especially in the older age group, and by achieving the unlikely state of technical perfection.

We would like to thank members of the West Midlands Surgical Society who allowed the notes of their patients to be studied. The co-operation of Mrs. Wall, at the statistics department, Birmingham Regional Hospital Board, is also appreciated.

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References

Dawson-Edwards, P., and Morrissey, D. M. (1954). *British Journal of Surgery*, 42, 643.
Eisenberg, M. M., Woodward, E. R., Carson, T. J., and Dragstedt, L. R. (1969). *Annals of Surgery*, 170, 317.
Goligher, J. C., *et al.* (1968a). *British Medical Journal*, 2, 781.
Goligher, J. C., *et al.* (1968b). *British Medical Journal*, 2, 787.
Mead, P. H. (1967). *American Journal of Surgery*, 114, 910.
Price, J. J., Powis, S. J. A., and Morrissey, D. M. (1972). Submitted for publication.
Savage, L. E., and McVay, C. B. (1970). *American Journal of Surgery*, 119, 191.
Small, W. T., and Jahadi, M. R. (1970). *American Journal of Surgery*, 119, 372.
Whittaker, L. D., Judd, E. S., and Stauffer, M. H. (1967). *Surgery, Gynecology and Obstetrics with International Abstracts of Surgery*, 125, 1081.

Pernicious Anaemia and Rheumatoid Arthritis

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Summary

In a study of 99 patients with pernicious anaemia the incidence of clinical rheumatoid arthritis was normal but rheumatoid factor was present significantly more often than in controls. This was not related to the presence of circulating antibody to intrinsic factor.

Intrinsic factor antibody was not detected in any of 151 latex-fixation-positive rheumatoid sera.

Introduction

There is probably an increased incidence of megaloblastic anaemia in rheumatoid arthritis (Chanarin, 1969). In a large retrospective survey by Partridge and Duthie (1963), involving 2,544 patients with rheumatoid arthritis and 5,515 controls, macrocytic-megaloblastic anaemia was five times more common in the rheumatoid group. This was ascribed largely to Addisonian pernicious anaemia (P.A.) by the authors. Bieder and Wigley (1964) found two cases of P.A. in a group of 20 patients with rheumatoid arthritis. But other studies by Gough *et al.* (1964), Deller *et al.* (1966), and Carter *et al.* (1968) did not confirm this increased frequency of P.A. in rheumatoid arthritis.

Conversely the incidence of rheumatoid arthritis in P.A. has not received much attention. Rheumatoid arthritis was not mentioned by Wilkinson (1933) in his review of diseases associated with P.A. Wangel *et al.* (1968) found eight patients with rheumatoid arthritis among 132 with P.A.

This report presents a study of the association of rheumatoid arthritis and P.A. and the frequency with which circulating intrinsic factor antibody and rheumatoid factor occur in the two conditions.

Patients and Methods

Table I gives the numbers and ages of patients studied. Those with P.A. were regular attenders at the haematology outpatient department, United Sheffield Hospitals. The diagnostic criteria for P.A. included a history of megaloblastic anaemia (without previous gastric surgery) completely responding to vitamin B_{12} therapy, achlorhydria and/or absent or virtually absent intrinsic factor secretion on maximal gastric stimulation, and abnormal Schilling test improving significantly with a suitable dose of intrinsic factor. In each case the patient was examined by me for evidence of rheumatoid arthritis and serum tested for rheumatoid factor and intrinsic factor antibody.

TABLE I—*Ages of Patients Studied*

	No.			Age in Years			
				Range		Mean	
	Men	Women	Total	Men	Women	Men	Women
Pernicious anaemia	40	59	99	30-91	30-85	65·2	66·2
Latex-positive rheumatoid arthritis	61	90	151	16-73	23-76	53·6	52·1
Controls	87	95	182	13-92	15-92	59·7	53·8

From a large number of blood samples sent for latex fixation tests to the department of haematology, United Sheffield Hospitals, 151 rheumatoid-factor-positive sera were taken. All latex-positive sera where the blood samples had been accompanied by a clinical diagnosis of rheumatoid arthritis were included in this study. The patients concerned were not examined by me. In each case the serum was tested for intrinsic factor antibody.

The 182 controls were individuals without evidence of P.A., rheumatoid arthritis, diabetes mellitus, or thyroid disease. Nearly two-thirds of these were ambulant hospital outpatients and the rest inpatients. Their sera were examined for both rheumatoid factor and intrinsic factor antibody.

Intrinsic factor antibody was detected by a modified charcoal absorption method (Ghazi, 1972) in which the amount of bound vitamin B_{12} in a sequence of gastric juice (normal) + ^{57}Co B_{12} + test serum is compared with that of gastric juice + test serum + ^{57}Co B_{12}. Sera inhibiting B_{12} uptake of gastric juice by more than 5 ng/ml were regarded as antibody-positive. Rheumatoid factor was detected by slide agglutination at serum dilutions of 1/25 with human IgG-coated latex suspension (Wellcotest).

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Results and Discussion

RHEUMATOID ARTHRITIS AND RHEUMATOID FACTOR IN P.A.

Only 5 of the 99 patients with P.A. had clinical rheumatoid arthritis. This is no more than the incidence of clinical rheumatoid arthritis in a survey of the general population of Leigh, Wensleydale, and Watford by Kellgren (1966). All five of our P.A. patients with rheumatoid arthritis were women over the age of 50 (Table II). With the exception of Case 5 the arthritis was not severe and there was no other coexistent autoimmune disease. There did not seem to be any correlation between the duration of P.A. and the development of rheumatoid arthritis.

TABLE II—*Data Concerning Five P.A. Patients with Rheumatoid Arthritis*

Case No.	Age and Sex	Duration of P.A.	Rh. Arthritis		Associated Autoimmune Disease	Latex Fixation	Intrinsic Factor Antibody
			Duration	Severity			
1	74 F.	3 years	10 years	Mild	0	−	+
2	71 F.	3 years	18 months	Mild	0	+	−
3	79 F.	12 years	5 years	Mild	0	−	−
4	69 F.	4 years	5 years	Mild	0	−	+
5	58 F.	11 years	6 years	Severe	Diabetes mellitus. Myxoedema	+	+

As shown in Table III, there was a significantly greater incidence of rheumatoid factor in patients with P.A. (11 out of 99) than in controls (7 out of 182). As this might have been due to disparity in the ages of the two groups (Table I) all subjects below the age of 50 were excluded and a further statistical comparison was made. Again the frequency of rheumatoid factor in P.A. was found to be significantly greater (Table IV). Two of the 11 P.A. patients with rheumatoid factor (including Case 5 in Table II) had myxoedema, but none had any conditions (other than rheumatoid arthritis in two cases)—for example, systemic lupus erythematosus, syphilis, yaws, septicaemia, etc.—known to be associated with a higher incidence of rheumatoid factor. A possible association between circulating intrinsic factor antibody and rheumatoid factor was studied (Table V) but rheumatoid factor was not found significantly more often in intrinsic-factor-antibody-positive P.A. sera compared with the antibody-negative P.A. sera.

TABLE III—*Incidence of Rheumatoid Factor*

	No.			Latex Positive		
	Men	Women	Total	Men	Women	Total
Pernicious anaemia ..	40	59	99	5	6	11
Controls	87	95	182	4	3	7
				$\chi^2 = 5{\cdot}65$. $P = 0{\cdot}025 - 0{\cdot}010$		

TABLE IV—*Incidence of Rheumatoid Factor in Patients Aged over 50*

		No.		Age in Years		Latex Positive	
				Range	Mean		
P.A.	Men	38	94	50-91	66·9	5	11
	Women	56		50-85	69·5	6	
Controls	Men	63	115	50-92	69·5	2	5
	Women	52		53-92	71·3	3	
						$\chi^2 = 3{\cdot}94$. $P = 0{\cdot}05 - 0{\cdot}02$	

TABLE V—*Incidence of Rheumatoid Factor in Intrinsic-factor-antibody-positive Sera Compared with Intrinsic-factor-antibody-negative Sera*

Pernicious Anaemia	No.	Latex-positive
Intrinsic factor antibody positive ..	51	7
Intrinsic factor antibody negative ..	48	4
	$\chi^2 = 0{\cdot}73$. $P = 0{\cdot}40 - 0{\cdot}30$	

INTRINSIC FACTOR ANTIBODY IN RHEUMATOID ARTHRITIS

Intrinsic factor antibody was not detected in any of the 151 latex-positive rheumatoid sera and 182 controls, whereas it was present in more than 50% of P.A. sera (Table VI). Intrinsic factor antibody is almost pathognomonic of P.A. and is rarely found in patients without P.A. However, a large percentage of patients with P.A. are intrinsic-factor-antibody-negative, which limits its diagnostic usefulness. Nevertheless its absence in all 151 latex-positive rheumatoid sera suggests that the incidence of P.A. in rheumatoid arthritis is not particularly high.

TABLE VI—*Incidence of Intrinsic Factor Antibody*

	No.		Intrinsic Factor Antibody Positive		
	Men	Women	Men	Women	Total
Latex-positive rheumatoid arthritis	61	90	0	0	0
Controls	87	95	0	0	0
Pernicious anaemia	40	59	18	33	51

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References

Bieder, L., and Wigley, R. D. (1964). *New Zealand Medical Journal*, **63**, 375.
Carter, M. E., Ardeman, S., Winocour, V., Perry, J., and Chanarin, I. (1968). *Annals of the Rheumatic Diseases*, **27**, 454.
Chanarin, I. (1969). *The Megaloblastic Anaemias*. Oxford, Blackwell Scientific.
Deller, D. J., *et al.* (1966). *British Medical Journal*, **1**, 765.
Ghazi, H. A. (1972). To be published.
Gough, K. R., McCarthy, C., Read, A. E., Mollin, D. L., and Waters, A. H. (1964). *British Medical Journal*, **1**, 212.
Kellgren, J. H. (1966). *Arthritis and Rheumatism*, **9**, 658.
Partridge, R. E. H., and Duthie, J. J. R. (1963). *British Medical Journal*, **1**, 89.
Wangel, A. G., *et al.* (1968). *British Journal of Haematology*, **14**, 161.
Wilkinson, J. F. (1933). *Quarterly Journal of Medicine*, **26**, 281.